



DOCKET NO.: ISIS-1158

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I hereby patent application of:

Nielsen, et al.

Serial No.: 08/319,411

Group No.: Not yet assigned.

Filed: October 6, 1994

Examiner: Not yet assigned.

For: Peptide Nucleic Acid Conjugates

Commissioner of Patents & Trademarks  
Washington, DC 20231

Sir:

ASSOCIATE POWER OF ATTORNEY

The undersigned, John W. Caldwell, Registration No. 28,937, of the firm WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, Attorney and/or Agent for Applicant(s), hereby appoints the following:

|                        |                         |
|------------------------|-------------------------|
| Robert B. Washburn     | Registration No. 16,574 |
| Richard E. Kurtz       | Registration No. 19,263 |
| John J. Mackiewicz     | Registration No. 19,709 |
| Norman L. Norris       | Registration No. 24,196 |
| Albert W. Preston, Jr. | Registration No. 25,366 |
| Dale M. Heist          | Registration No. 28,425 |
| Philip S. Johnson      | Registration No. 27,200 |
| Gary H. Levin          | Registration No. 28,734 |
| Steven J. Rocci        | Registration No. 30,489 |
| Dianne B. Elderkin     | Registration No. 28,598 |
| Francis A. Paintin     | Registration No. 19,386 |
| John P. Donohue, Jr.   | Registration No. 29,916 |
| Henrik D. Parker       | Registration No. 31,863 |

|                       |                          |
|-----------------------|--------------------------|
| Suzanne E. Miller     | Registration No. 32,279  |
| Lynn B. Morreale      | Registration No. 32,842  |
| Albert T. Keyack      | Registration No. 32,906  |
| Joseph Lucci          | Registration No. 33,307  |
| Michael P. Dunnam     | Registration No. 32,611  |
| Michael D. Stein      | Registration No. 34,734  |
| Albert J. Marcellino  | Registration No. 34,664  |
| David R. Bailey       | Registration No. 35,057  |
| Rebecca L. Ralph      | Registration No. 35,152  |
| John L. Knoble        | Registration No. 32,387  |
| Michele K. Herman     | Registration No. 35,893  |
| Barbara L. Mullin     | Registration No. 38,250  |
| Ken I. Yoshida        | Registration No. 37,009  |
| Mark DeLuca           | Registration No. 33,229  |
| Steven B. Samuels     | Registration No. 37,711  |
| Lynn A. Malinoski     | Registration No. P38,788 |
| Lori Y. Beardell      | Registration No. 34,293  |
| Frederick A. Tecce    | Registration No. 32,065  |
| Raymond M. Speer      | Registration No. 26,810  |
| Doreen Yatko Trujillo | Registration No. 35,719  |
| Kathryn Leary         | Registration No. 36,317  |
| Michael P. Straher    | Registration No. 38,325  |
| Merle W. Richman, III | Registration No. 38,282  |
| Paul K. Legaard       | Registration No. 38,534  |
| Kevin M. Flannery     | Registration No. 35,871  |
| David A. Cherry       | Registration No. 35,099  |
| Anthony J. Rossi      | Registration No. 24,053  |
| D. Jennings Meincke   | Registration No. 36,606  |

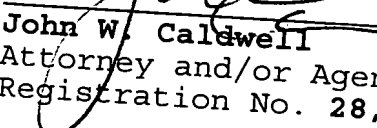
and

|                  |                         |
|------------------|-------------------------|
| Herb Boswell     | Registration No. 27,311 |
| Laurel Bernstein | Registration No. 37,280 |

of **ISIS PHARMACEUTICALS**, 2280 Faraday Avenue, Carlsbad, California 92008; his associates, with full power to prosecute the above-identified application and to transact all business in the Patent Office connected therewith and requests that

correspondence continue to be directed to the firm of WOODCOCK  
WASHBURN KURTZ MACKIEWICZ & NORRIS at the above address.

Date: April 10, 1995

  
John W. Caldwell  
Attorney and/or Agent of Record  
Registration No. 28,937

WOODCOCK WASHBURN KURTZ  
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One Liberty Place - 46th Floor  
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COMBINED DECLARATION AND POWER OF ATTORNEY

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( ) is attached hereto.

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I hereby claim foreign priority benefits under 35 U.S.C. § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of any application on which priority is claimed:

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|----------------|-----------------|-----------------------|------------------|
| <u>PCT</u>     | <u>EP/01219</u> | <u>May 22, 1992</u>   | <u>Yes.</u>      |
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| <u>Denmark</u> | <u>510/92</u>   | <u>April 15, 1992</u> | <u>Yes.</u>      |

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

| Application Serial No. | Filing Date            | Status (patented, pending) |
|------------------------|------------------------|----------------------------|
| <u>08/108,591</u>      | <u>August 27, 1993</u> | <u>pending</u>             |
| <u>08/088,658</u>      | <u>July 2, 1993</u>    | <u>pending</u>             |
| <u>08/088,661</u>      | <u>July 2, 1993</u>    | <u>pending</u>             |
| <u>08/275,951</u>      | <u>July 15, 1994</u>   | <u>pending</u>             |

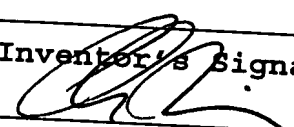
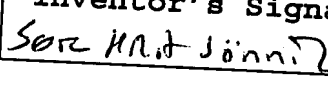
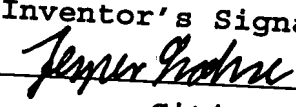
3 I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: **John W. Caldwell**, Registration No. 28,937, of the firm of **WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS**, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, and **Herb Boswell and Laurel Bernstein**, Registration Nos. 27,311 and 37,280, of **ISIS Pharmaceuticals**, 2280 Faraday Avenue, Carlsbad, California 92008.

Address all telephone calls and correspondence to:

John W. Caldwell, Esquire  
WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS  
One Liberty Place - 46th Floor  
Philadelphia, PA 19103  
Telephone No. 215-568-3100.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

|   |   |  |                                   |
|---|---|--|-----------------------------------|
| 1 | Full Name<br><u>Peter Nielsen</u>                     | Inventor's Signature<br>   | Date<br>6/1-95                    |
|   | Residence<br>DK 2980 <u>Kokkedal</u> , Denmark DKX    |  | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Hjortevanget 509               |  |                                   |
| 2 | Full Name<br><u>Ole Buchardt</u>                      | Inventor's Signature   | Date                              |
|   | Residence<br>DK 3500 <u>Vaerlose</u> , Denmark        |  | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Søndergardsvej 73              |  |                                   |
| 3 | Full Name<br><u>Søren Holst Sonnechsen</u>            | Inventor's Signature<br>  | Date<br>6/1/1995                  |
|   | Residence<br>DK 2630 <u>Tastrup</u> , Denmark DKX     |  | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Gronhojgardsvej 13             |  |                                   |
| 4 | Full Name<br><u>Jesper Lohse</u>                      | Inventor's Signature<br> | Date<br>6/1/1995                  |
|   | Residence<br>DK 2400 <u>Copenhagen N</u> Denmark, DKX |  | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Staerevej 52, 2.tv,            |  |                                   |
| 5 | Full Name<br><u>Michael Egholm</u>                    | Inventor's Signature   | Date                              |
|   | Residence<br><u>Lexington, MA 02173</u>               |  | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>1231 Lexington Ridge Drive     |  |                                   |

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|     |    |   |  |                 |
|-----|----|---|--|-----------------|
| 680 | 6  | Full Name<br><u>Muthiah Manoharan</u>               | Inventor's Signature<br><u>Muthiah Manoharan</u> | Date<br>1/20/95 |
|     |    | Residence<br><u>Carlsbad, CA 92009</u> CA           | Citizenship<br>U.S.A.                            |                 |
|     |    | Post Office Address<br>7634 Reposado Drive          |  |                 |
| 780 | 7  | Full Name<br><u>John Kiely</u>                      | Inventor's Signature<br><u>John Kiely</u>        | Date<br>1/16/95 |
|     |    | Residence<br><u>San Diego, CA 92130</u> CA          | Citizenship<br>U.S.A.                            |                 |
|     |    | Post Office Address<br>4230 Corte Facil             |  |                 |
| 800 | 8  | Full Name<br><u>Michael Griffith</u>                | Inventor's Signature<br><u>Michael Griffith</u>  | Date<br>1/20/95 |
|     |    | Residence<br><u>San Diego, CA 92130</u> CA          | Citizenship<br>U.S.A.                            |                 |
|     |    | Post Office Address<br>3686 Carmel Landing          |  |                 |
| 900 | 9  | Full Name<br><u>Kelly Sprankle</u>                  | Inventor's Signature<br><u>Kelly Sprankle</u>    | Date<br>1/20/95 |
|     |    | Residence<br><u>Vista, CA 92083</u> CA              | Citizenship<br>U.S.A.                            |                 |
|     |    | Post Office Address<br>920 Sycamore Avenue, Apt. 61 |  |                 |
| 10  | 10 | Full Name   | Inventor's Signature                             | Date            |
|     |    | Residence   | Citizenship                                      |                 |
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|---|--|---|-----------------------------------|
| 1 | Full Name<br>Peter Nielsen                       | Inventor's Signature                          | Date                              |
|   | Residence<br>DK 2980 Kokkedal, Denmark           |   | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Hjortevanget 509          |   |                                   |
| 2 | Full Name<br>Ole Buchardt                        | Inventor's Signature                          | Date                              |
|   | Residence<br>DK 3500 Vaerlose, Denmark           |   | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Sondergardsvej 73         |   |                                   |
| 3 | Full Name<br>Soren Holst Sonnichsen              | Inventor's Signature                          | Date                              |
|   | Residence<br>DK 2630 Tastrup, Denmark            |   | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Gronhojgardsvej 13        |   |                                   |
| 4 | Full Name<br>Jesper Lohse                        | Inventor's Signature                          | Date                              |
|   | Residence<br>DK 2400 Copenhagen N Denmark,       |   | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Staerevej 52, 2.tv,       |   |                                   |
| 5 | Full Name<br>Michael Egholm <i>5-0</i>           | Inventor's Signature<br><i>Michael Egholm</i> | Date<br>4/10/95                   |
|   | Residence<br>Lexington, MA 02173 <i>ML</i>       |   | Citizenship<br>Citizen of Denmark |
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|   |   |                      |                                   |
| 4 | Full Name<br>Jesper Lohse                         | Inventor's Signature | Date                              |
|   | Residence<br>DK 2400 Copenhagen N Denmark,        |                      | Citizenship<br>Citizen of Denmark |
|   | Post Office Address<br>Staerevej 52, 2.tv,        |                      |                                   |
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|   | Residence<br>Lexington, MA 02173                  |                      | Citizenship<br>Citizen of Denmark |
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| 6  | Full Name<br>Muthiah Manoharan                      | Inventor's Signature | Date                  |
|    | Residence<br>Carlsbad, CA 92009                     |                      | Citizenship<br>U.S.A. |
|    | Post Office Address<br>7634 Reposado Drive          |                      |                       |
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|    | Residence<br>San Diego, CA 92130                    |                      | Citizenship<br>U.S.A. |
|    | Post Office Address<br>4230 Corte Facil             |                      |                       |
| 8  | Full Name<br>Michael Griffith                       | Inventor's Signature | Date                  |
|    | Residence<br>San Diego, CA 92130                    |                      | Citizenship<br>U.S.A. |
|    | Post Office Address<br>3686 Carmel Landing          |                      |                       |
| 9  | Full Name<br>Kelly Sprankle                         | Inventor's Signature | Date                  |
|    | Residence<br>Vista, CA 92083                        |                      | Citizenship<br>U.S.A. |
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#9  
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I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

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I hereby claim foreign priority benefits under 35 U.S.C. § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of any application on which priority is claimed:

| Country        | Number          | Date Filed            | Priority Claimed |
|----------------|-----------------|-----------------------|------------------|
| <u>PCT</u>     | <u>EP/01219</u> | <u>May 22, 1992</u>   | <u>Yes.</u>      |
| <u>Denmark</u> | <u>986/91</u>   | <u>May 24, 1991</u>   | <u>Yes.</u>      |
| <u>Denmark</u> | <u>987/91</u>   | <u>May 24, 1991</u>   | <u>Yes.</u>      |
| <u>Denmark</u> | <u>510/92</u>   | <u>April 15, 1992</u> | <u>Yes.</u>      |



I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

| Application Serial No. | Filing Date            | Status (patented, pending) |
|------------------------|------------------------|----------------------------|
| <u>08/108,591</u>      | <u>August 27, 1993</u> | <u>pending</u>             |
| <u>08/088,658</u>      | <u>July 2, 1993</u>    | <u>pending</u>             |
| <u>08/088,661</u>      | <u>July 2, 1993</u>    | <u>pending</u>             |
| <u>08/275,951</u>      | <u>July 15, 1994</u>   | <u>pending</u>             |

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: John W. Caldwell, Esquire Registration No. 28,937 of the firm of WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, and Herb Boswell and Laurel Bernstein, Registration Nos. 27,311 and 37,280, of ISIS Pharmaceuticals, 2280 Faraday Avenue, Carlsbad, California 92008.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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| 1 | Full Name<br>Peter Nielsen                        | Inventor's Signature                          | Date            |
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| 4 | Full Name<br>Jesper Lohse                         | Inventor's Signature                          | Date            |
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| 5 | Full Name<br>Michael Egholm                       | Inventor's Signature<br><i>Michael Egholm</i> | Date<br>4/10/95 |
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|----|---|----------------------|-----------------------|
| 6  | Full Name<br>Muthiah Manoharan                      | Inventor's Signature | Date                  |
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| 7  | Full Name<br>John Kiely                             | Inventor's Signature | Date                  |
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| 8  | Full Name<br>Michael Griffith                       | Inventor's Signature | Date                  |
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|    | Post Office Address<br>3686 Carmel Landing          |                      |                       |
| 9  | Full Name<br>Kelly Sprankle                         | Inventor's Signature | Date                  |
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|    | Post Office Address<br>920 Sycamore Avenue, Apt. 61 |                      |                       |
| 10 | Full Name   | Inventor's Signature | Date                  |
|    | Residence   |                      | Citizenship           |
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DOCKET NO.: ISIS-1158

PATENT

## COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and

I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: Peptide Nucleic Acid Conjugates, the specification of which:

(XX) was filed on October 6, 1994, as Application Serial No. 08/319,411.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the U.S. Patent and Trademark Office all information known to be material to the patentability of this application in accordance with 37 CFR § 1.56.

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| 1 | Full Name<br>Peter Nielsen                                 | Inventor's Signature                       | Date           |
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| 3 | Full Name<br>Soren Holst Sonnichsen                        | Inventor's Signature                       | Date           |
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| 4 | Full Name<br>Jesper Lohse                                  | Inventor's Signature                       | Date           |
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| 5 | Full Name<br>Michael Egholm                                | Inventor's Signature                       | Date           |
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| 6  | Full Name<br>Muthiah Manoharan                      | Inventor's Signature | Date                  |
|    | Residence<br>Carlsbad, CA 92009                     |                      | Citizenship<br>U.S.A. |
|    | Post Office Address<br>7634 Reposado Drive          |                      |                       |
| 7  | Full Name<br>John Kiely                             | Inventor's Signature | Date                  |
|    | Residence<br>San Diego, CA 92130                    |                      | Citizenship<br>U.S.A. |
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| 8  | Full Name<br>Michael Griffith                       | Inventor's Signature | Date                  |
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| 10 | Full Name   | Inventor's Signature | Date                  |
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